Ushamed TOTAL 09/886311

=5 fil reg COST IN U.S. DOLLARS

SINCE FILE ENTRY

0.21

TOTAL SESSION 0.21

\*FULL ESTIMATED COST

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=> e exendin	/cn 5	
E1	1	EXEMESTANE/CN
E2	1	EXENATIDE/CN
E3	1>	EXENDIN/CN
E4		EXENDIN 3/CN
E5		EXENDIN 3 (HELODERMA HORRIDUM)/CN
=> e		
E6	1	EXENDIN 3 (HELODERMA HORRIDUM), 1-DE-L-HISTIDINE-2-DE-L-SERI
	-	NE-3-DE-L-ASPARTIC ACID-4-DEGLYCINE-5-DE-L-THREONINE-6-DE-L-
		PHENYLALANINE-7-DE-L-THREONINE-8-DE-L-SERINE-/CN
E7	1	EXENDIN 3 (HELODERMA HORRIDUM), 2-GLYCINE-/CN
E8	1	EXENDIN 3 (HELODERMA HORRIDUM), 2-GLYCINE-3-L-GLUTAMIC ACID-
120	1	/CN / CN
E9	1	·
ĽЭ	1	EXENDIN 3 (HELODERMA HORRIDUM), 2-GLYCINE-3-L-GLUTAMIC ACID-
п10	-	39-(3,5-DI(IODO-125I)-L-TYROSINE)-/CN
E10	1	EXENDIN 3 (HELODERMA HORRIDUM), 2-GLYCINE-3-L-GLUTAMIC ACID-
D44	_	39-(3-(IODO-125I)-L-TYROSINE)-/CN
E11	1	EXENDIN 3 (HELODERMA HORRIDUM), 2-GLYCINE-3-L-GLUTAMIC ACID-
		39-L-TYROSINAMIDE-/CN
E12	1	EXENDIN 3 (HELODERMA HORRIDUM), 39A-(N6-(15-(2,5-DIHYDRO-2,5
		-DIOXO-1H-PYRROL-1-YL)-1,7,13-TRIOXO-3,9-DIOXA-6,12-DIAZAPEN
		TADEC-1-YL)-L-LYSINAMIDE)-/CN
E13	1	EXENDIN 3 (HELODERMA HORRIDUM), 39A-(N6-(15-(2,5-DIHYDRO-2,5
		-DIOXO-1H-PYRROL-1-YL)-1,7,13-TRIOXO-3,9-DIOXA-6,12-DIAZAPEN
		TADEC-1-YL)-L-LYSINAMIDE)-, PENTAKIS(TRIFLUOROACETATE) (SALT
		)/CN
E14	1	EXENDIN 3 (HELODERMA HORRIDUM), 39A-(N6-(21-(2,5-DIHYDRO-2,5
		-DIOXO-1H-PYRROL-1-YL)-1,10,19-TRIOXO-3,6,12,15-TETRAOXA-9,1
		8-DIAZAHENEICOS-1-YL)-L-LYSINAMIDE)-/CN
E15	1	EXENDIN 3 (HELODERMA HORRIDUM), 39A-(N6-(21-(2,5-DIHYDRO-2,5
		-DIOXO-1H-PYRROL-1-YL)-1,10,19-TRIOXO-3,6,12,15-TETRAOXA-9,1
		8-DIAZAHENEICOS-1-YL)-L-LYSINAMIDE)-, PENTAKIS (TRIFLUOROACET
		ATE) (SALT)/CN
		, (, ,

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F16
                   EXENDIN 3 (HELODERMA HORRIDUM), 39A-(N6-(3-(2,5-DIHYDRO-2,5-
                   DIOXO-1H-PYRROL-1-YL)-1-OXOPROPYL)-L-LYSINAMIDE)-/CN
E17
                   EXENDIN 3 (HELODERMA HORRIDUM), 39A-(N6-(3-(2,5-DIHYDRO-2,5-
                   DIOXO-1H-PYRROL-1-YL)-1-OXOPROPYL)-L-LYSINAMIDE)-, PENTAKIS (
                   TRIFLUOROACETATE) (SALT)/CN
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L2
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
     130391-54-7 REGISTRY
CN
     Exendin 3 (9CI) (CA INDEX NAME)
MF
     Unspecified
CI
     MAN
SR
LC
     STN Files:
                  ADISINSIGHT, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT,
       CAPLUS, CHEMCATS, EMBASE, MEDLINE, MRCK*, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
       Roles from patents: BIOL (Biological study); PREP (Preparation); PROC
RL.P
       (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
       Roles for non-specific derivatives from patents: BIOL (Biological
RLD.P
       study); PREP (Preparation); USES (Uses)
       Roles from non-patents: BIOL (Biological study); PROC (Process); PRP
RL.NP
       (Properties); USES (Uses)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
              27 REFERENCES IN FILE CA (1907 TO DATE)
               3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
              27 REFERENCES IN FILE CAPLUS (1907 TO DATE)
REFERENCE 1: 140:363055 Microencapsulation and sustained release of
     biologically active polypeptides. Costantino, Henry R.; Hotz, Joyce
     (Alkermes Controlled Therapeutics, Inc. II, USA). PCT Int. Appl. WO
     2004036186 A2 20040429, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT,
     AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM,
     DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
     KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
     MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
     SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM,
     AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK,
     ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD,
     TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US33168
     20031017. PRIORITY: US 2002-PV419388 20021017.
    This invention relates to compns. for the sustained release of biol.
AΒ
     active polypeptides, and methods of forming and using said compns., for
     the sustained release of biol. active polypeptides, such as glucagon,
    glucagon-like peptides, exendins, vasoactive intestinal peptide, Igs,
    antibodies, cytokines, interleukins, macrophage activating factors,
    interferons, erythropoietin tumor necrosis factor, colony stimulating
    factors, hormones, etc. The sustained release compns. of this invention
    comprise a biocompatible polymer having dispersed therein, a biol. active
    polypeptide, a sugar and a salting-out salt. For example, exendin-4 was
    encapsulated in poly(lactide-co-glycolide) using a water-oil-oil (W/O/O)
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emulsion system. The initial embryonic microparticles were formed in a W/O/O inner emulsion step after which they were subjected to coacervation and hardening steps. The inner phase was prepared by dissolving the exendin-4, sucrose and ammonium sulfate in water or an aqueous buffer and injected into a polymer phase (PLG dissolved in methylene chloride) while sonicating. The resultant water/oil emulsion was then mixed with silicone oil, and the mixture was added to heptene to form microparticles. The microparticles were collected, dried and filled into vials.

- REFERENCE 2: 140:363053 Microencapsulation and sustained release of biologically active polypeptides. Costantino, Henry R.; Hotz, Joyce (Alkermes Controlled Therapeutics, Inc. II, USA). PCT Int. Appl. WO 2004035754 A2 20040429, 72 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US33062 20031017. PRIORITY: US 2002-PV419388 20021017.
- This invention relates to compns. for the sustained release of biol. AB active polypeptides, and methods of forming and using said compns., for the sustained release of biol. active polypeptides. The sustained release compns. of this invention comprise a biocompatible polymer having dispersed therein, a biol. active polypeptide, a sugar and a salting-out For example, exendin-4 was encapsulated in poly(lactide-coglycolide) (PLG) polymer using a water-oil-oil (W/O/O) emulsion system. The initial embryonic microparticles were formed in a W/O/O inner emulsion step after which they were subjected to coacervation and hardening steps. A water-in-oil emulsion was created using sonication. The water phase of the emulsion contained dissolved exendin-4 and excipients, e.g., sucrose and ammonium sulfate, while the PLG phase contained polymer dissolved in methylene chloride. The aqueous solution was then injected into the polymer solution while sonicating. The resultant water/oil emulsion was then mixed with silicone oil and the mixture was added to n-heptane to form microparticles. The microparticles were isolated by filtration and vacuum dried.
- REFERENCE 3: 140:317698 Method for producing acylated peptides. Duenweber, Dorte Lunoe; Jensen, Inge Holm; Hansen, Louis Brammer (Novo Nordisk A/S, Den.). PCT Int. Appl. WO 2004029077 A2 20040408, 24 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-DK629 20030925. PRIORITY: DK 2002-1421 20020925.

  AB The present invention provides a method for acylating one or more amino groups of a peptide where the acylation reaction is to be performed in an aqueous mixture containing less than 10 %weight/weight aprotic polar solvent.

Arg34GLP-1(7-37) was dissolved in 0.1 mol/kg triethylamine (23 mL) at 10-15 °C. N-hexadecanoylglutamic acid  $\gamma\text{-N-hydroxysuccinimide}$  ester (63.7 mg, 0.13 mmol) was added. After 20 min at room temperature water (42 mL) was added, and the pH was adjusted to 8.0 by addition of 1.0 M acetic acid. The reaction mixture was shown to contain 84 % (by area) of Arg34Lys26-[N- $\epsilon$ -[ $\gamma$ -Glu(N-hexadecanoyl)]]-GLP-1(7-37) and 0.5

Recombinant

% (by area) of Arg34Lys26-[N- $\epsilon$ -( $\alpha$ -Glu(N-hexadecanoyl))]-GLP-1(7-37).

\*REFERENCE 4: 140:157460 PPARα-selective chromane and chromene compounds for the treatment of dyslipidemia and other lipid disorders, and preparation thereof. Desai, Ranjit C.; Sahoo, Soumya (Merck & Co., Inc., USA). PCT Int. Appl. WO 2004010992 A1 20040205, 57 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US23499 20030725. PRIORITY: US 2002-PV399518 20020730.

GΙ

AB A class of chromane and chromene compds. I [R1, R2, R4 = (un)substituted C1-3 alkyl; R3, R5, R7 = H, (un)substituted C1-3 alkyl; R6 = H, C1, Me, CF3; A, B = H, C1, F, Me, CF3; X, Y = O, S; n = 2, 3; dashed line = optional double bond], and pharmaceutically acceptable salts thereof, are useful as therapeutic compds., particularly in the treatment and control of hyperlipidemia, hypercholesterolemia, dyslipidemia, and other lipid disorders, and in delaying the onset of or reducing the risk of conditions and sequelae that are associated with these diseases, such as atherosclerosis. Compound preparation is included.

REFERENCE 5: 140:123175 Multi-step method and media compositions for the differentiation of stem cells into insulin-producing cells, formation of pancreatic islets and therapeutics uses thereof. Clarke, Diana; D'Alessandro, Josephine S.; Lu, Kuanghui; Wang, Anlai (ES Cell International Pte. Ltd., Singapore). PCT Int. Appl. WO 2004011621 A2 20040205, 77 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US23852 20030729. PRIORITY: US 2002-PV399476 20020729; US 2002-PV409847 20020911; US 2003-PV452732 20030307.

AB The present invention provides improved methods of differentiating insulin+, glucose responsive islet-like structures from insulin- cells. The invention further provides methods for using insulin+, glucose responsive islet-like structures, as well as the insulin+, glucose responsive cells which comprise said islet-like clusters.

REFERENCE 6: 140:105831 Pharmaceutical compositions and uses of GLP-1 mimetics for the treatment of diabetes. Steiness, Eva (Zealand Pharma A/S, Den.). PCT Int. Appl. WO 2004005342 Al 20040115, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-DK463 20030702. PRIORITY: US 2002-PV393917 20020704; US 2003-PV465613 20030424.

The present invention relates to use of GLP-1 or a related mol. having GLP-effect for the manufacture of a medicament for preventing or treating diabetes in a mammal. The amount and timing of administration of said medicament are subsequently reduced to produce a 'drug holiday'. Practice of the invention achieves effective therapy without continuous drug exposure and without continuous presence of therapeutic levels of the drug. The invention also discloses a method of treating diabetes and related disorders in a mammal by administering glucagon like peptide (GLP-1) or a related mol. having GLP-1 like effect and thereby providing a therapeutically effective amount of endogenous insulin.

REFERENCE 7: 140:26964 Use of the lantibiotic transport system to secrete foreign proteins into culture medium for purification. Moll, Gert Nikolaas; Leenhouts, Cornelis Johannes; Kuipers, Oscar Paul; Driessen, Arnold Jacob Mathieu (Applied Nanosystems B.V., Neth.). PCT Int. Appl. WO 2003099862 A1 20031204, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-NL389 20030526. PRIORITY: EP 2002-77060 20020524; US 2003-360101 20030207. Methods of using the mechanisms involved in the secretion of lantibiotics AΒ to secrete foreign proteins from lantibiotic-producing hosts is described. The method can also be used to secrete lantibiotics before they have undergone post-translational modification, such as dehydration of a serine or a threonine, and/or thioether bridge formation, or to increase the efficiency of secretion of fully processed lantibiotics. A Lactococcus lactis strain lacking the entire nisin A biosynthetic gene cluster was transformed with a plasmid carrying the nisin A structural gene nisA and the transport protein nisT. This transgenic strain efficiently secreted the unmodified nisin A protein, indicating that lanT was sufficient to export the protein. Use of the signal peptide to direct secretion of an angiotensin variant is demonstrated. Use of the transport protein, the lantibiotic signal peptide, and the lantibiotic-modifying dehydrases and cyclases to manufacture novel variants of peptide hormones with modified amino is also demonstrated.

REFERENCE 8: 139:147766 Effects of preproglucagon-derived peptides and exendins on steroid-hormone secretion from dispersed adrenocortical cells of normal and streptozotocin-induced diabetic rats. Malendowicz, Ludwik K.; Spinazzi, Raffaella; Nussdorfer, Gastone G.; Trejter, Marcin (Department of Histology and Embryology, Karol Marcinkowski University of Medical Sciences, Poznan, PL-60781, Pol.). International Journal of Molecular Medicine, 12(1), 115-119 (English) 2003. CODEN: IJMMFG. ISSN:

1107-3756. Publisher: International Journal of Molecular Medicine. Many lines of evidence have shown that preproglucagon-derived peptides AΒ affect steroid secretion from dispersed adrenocortical cells, and that streptozotocin (STZ)-induced exptl. diabetes alters adrenocortical-cell function. Hence, we compared the effects of glucagon, glucagon-like peptide (GLP)-1 and GLP-2 on basal and ACTH-stimulated secretion of dispersed adrenocortical cells from normal and STZ-induced diabetic rats. We also examined the effects of exendins (EX) 3 and 4, because EX4 is known to be a potent and long-lasting agonist of GLP-1 receptors. STZ-induced diabetes moderately enhances basal and ACTH-stimulated secretion from dispersed zona glomerulosa (ZG) cells, without significantly affecting corticosterone production from dispersed zona fasciculata-reticularis (ZF/R) cells. In normoglycemic rats, glucagon increased basal aldosterone and corticosterone secretion from ZG and ZF/R cells, GLP-2 raised both basal and ACTH-stimulated aldosterone secretion and ACTH-stimulated corticosterone output, and EX4 increased basal corticosterone secretion. In contrast, glucagon, GLP-2 and EX4 did not elicit secretory responses from adrenocortical cells of diabetic rats. GLP-1 and EX3 did not alter secretion of dispersed adrenocortical cells of either normal or STZ-treated rats. Taken together, our findings indicate that preproglucagon-derived peptides enhance steroid secretion from adrenocortical cells of normal, but not STZ-induced diabetic rats. It is suggested that the prolonged exposure to low concns. of insulin causes unresponsiveness of adrenocortical cells to glucagon, GLP-2 and EX4, which may contribute to the hyporeninemie hypoaldosteronism and alterations in glucocorticoid metabolism occurring in exptl. diabetes.

REFERENCE 9: 139:26621 Medicinal compositions for nasal absorption.

Minamitake, Yoshiharu; Tsukada, Yoshio; Kanai, Yasushi; Yanagawa, Akira (Daiichi Suntory Pharma Co., Ltd., Japan; Dott Research Laboratory). PCT Int. Appl. WO 2003045418 Al 20030605, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2002-JP12337 20021126. PRIORITY: JP 2001-359559 20011126.

AB It is intended to provide medicinal compns. for nasal absorption which are excellent in the absorbability of a physiol. active polypeptide contained therein as the active ingredient in vivo in the case of the administration into the nasal cavity (nasal administration). More specifically, medicinal compns. for nasal absorption wherein an acidic physiol. active polypeptide having an isoelec. point of 7 or below is uniformly dispersed or embedded in a water-insol. or hardly water-soluble polyvalent metal compound carrier, for example, a bivalent or more metal compound such as an aluminum compound, a calcium compound, a magnesium compound, a silicon compound, an iron compound or a zinc compound with the use of an additive whereby the polypeptide can be dispersed or embedded in the carrier surface. For example, CaCO3 (average diameter 53.6 μm) and corn starch (average diameter

 $\mu$ m) were kneaded with distilled water and freeze-dried. The above product and 10.8 mg glucagon-like peptide I(7-37) were blended and kneaded with addition of an aqueous solution containing benzalkonium chloride. The product was dried

under reduced pressure and mixed with Ca stearate to give a powder for nasal administration.

REFERENCE 10: 138:332208 Induction of pancreatic  $\beta$  cell differentiation and insulin expression in human cells transformed for transcription factor

expression and a GLP-1 receptor agonist. Levine, Fred; Dufayet, Dominique; Itkin-Ansari, Pamela (The Regents of the University of California, USA). PCT Int. Appl. WO 2003032923 A2 20030424, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US33516 20021016. PRIORITY: US 2001-41845 20011018. AΒ The present invention provides methods for inducing insulin gene expression in cultured pancreas cells. A culture of endocrine pancreas cells are transformed for expression of a PDX-1 gene and a NeuroD/BETA2 gene with a GLP-1 receptor agonist. The cells have been cultured under conditions such that the cells are in contact with other cells in the culture, thereby inducing insulin gene expression in the cells. Thus, synergistic activation multiple signaling pathways results in differentiation of cultured human  $\beta$ -cells, which initially express no detectable pancreatic hormones, into fully functional  $\beta$ -cells that exhibit glucose-responsive insulin secretion. The invention also provides high-throughput screening methods for modulators of  $\beta$ -cell function, stable cultures of cells made by the methods of the invention, and methods of treating a human subject using the methods of the invention. The ability to grow unlimited quantities of functional human  $\beta$ -cells in vitro provides the means for a definitive cell transplantation therapy for treatment of diabetes. => e exendin/cn 5 1 EXEMESTANE/CN 1 E2 EXENATIDE/CN 1 --> EXENDIN/CN EЗ 1  ${
m E}\,4$ EXENDIN 3/CN EXENDIN 3 (HELODERMA HORRIDUM)/CN

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DT.CA CAplus document type: Journal; Patent
      Roles from patents: BIOL (Biological study); OCCU (Occurrence); PREP
       (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
      reagent); USES (Uses)
      Roles for non-specific derivatives from patents: BIOL (Biological
      study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological
      study); USES (Uses)
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- \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

  28 REFERENCES IN FILE CA (1907 TO DATE)

  8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

  28 REFERENCES IN FILE CAPLUS (1907 TO DATE)
- REFERENCE 1: 140:400083 Long-acting exendins and exendin agonists for the treatment of hyperglycemia and diabetes mellitus. Fridkin, Matityahu; Shechter, Yoram; Tsubery, Haim (Yeda Research and Development Co., Ltd, Israel). U.S. Pat. Appl. Publ. US 2004092443 Al 20040513, 15 pp., Cont.-in-part of U.S. Ser. No. 336,839. (English). CODEN: USXXCO. APPLICATION: US 2003-408262 20030408. PRIORITY: IL 1996-119029 19960807; WO 1997-IL265 19970805; US 1999-242026 19990205; US 2003-336839 20030106. AΒ Long-acting exendin or exendin agonist derivs. of the formula (X)nZ are provided [X = 9-fluorenylmethoxycarbonyl, 2-sulfo-9-fluorenylmethoxycarbonyl (FMS); Z = exendin residue or exendin agonist residue linked to X through amino or hydroxyl group; n = 1-3]. The exendin is exendin-3 or exendin-4. Preparation of (FMS)3-exendin-4 is described. derivs. are useful for prevention or treatment of conditions, diseases or disorders that can be treated by an exendin, e.g. for prevention of hyperglycemia and for treatment of diabetes mellitus, e.g. non-insulin dependent diabetes mellitus, insulin-dependent diabetes mellitus, and gestational diabetes mellitus.
- REFERENCE 2: 140:363055 Microencapsulation and sustained release of biologically active polypeptides. Costantino, Henry R.; Hotz, Joyce (Alkermes Controlled Therapeutics, Inc. II, USA). PCT Int. Appl. WO 2004036186 A2 20040429, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US33168 20031017. PRIORITY: US 2002-PV419388 20021017.
- AB This invention relates to compns. for the sustained release of biol. active polypeptides, and methods of forming and using said compns., for the sustained release of biol. active polypeptides, such as glucagon, qlucagon-like peptides, exendins, vasoactive intestinal peptide, Igs, antibodies, cytokines, interleukins, macrophage activating factors, interferons, erythropoietin tumor necrosis factor, colony stimulating factors, hormones, etc. The sustained release compns. of this invention comprise a biocompatible polymer having dispersed therein, a biol. active polypeptide, a sugar and a salting-out salt. For example, exendin-4 was encapsulated in poly(lactide-co-glycolide) using a water-oil-oil (W/O/O) emulsion system. The initial embryonic microparticles were formed in a W/O/O inner emulsion step after which they were subjected to coacervation and hardening steps. The inner phase was prepared by dissolving the exendin-4, sucrose and ammonium sulfate in water or an aqueous buffer and injected into a polymer phase (PLG dissolved in methylene chloride) while sonicating. The resultant water/oil emulsion was then mixed with silicone oil, and the mixture was added to heptene to form microparticles. The microparticles were collected, dried and filled into vials.
- REFERENCE 3: 140:363053 Microencapsulation and sustained release of biologically active polypeptides. Costantino, Henry R.; Hotz, Joyce (Alkermes Controlled Therapeutics, Inc. II, USA). PCT Int. Appl. WO 2004035754 A2 20040429, 72 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,

- MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US33062 20031017. PRIORITY: US 2002-PV419388 20021017.
- This invention relates to compns. for the sustained release of biol. active polypeptides, and methods of forming and using said compns., for the sustained release of biol. active polypeptides. The sustained release compns. of this invention comprise a biocompatible polymer having dispersed therein, a biol. active polypeptide, a sugar and a salting-out salt. For example, exendin-4 was encapsulated in poly(lactide-coglycolide) (PLG) polymer using a water-oil-oil (W/O/O) emulsion system. The initial embryonic microparticles were formed in a W/O/O inner emulsion step after which they were subjected to coacervation and hardening steps. A water-in-oil emulsion was created using sonication. The water phase of the emulsion contained dissolved exendin-4 and excipients, e.g., sucrose and ammonium sulfate, while the PLG phase contained polymer dissolved in methylene chloride. The aqueous solution was then injected into the polymer solution while sonicating. The resultant water/oil emulsion was then mixed with silicone oil and the mixture was added to n-heptane to form microparticles. The microparticles were isolated by filtration and vacuum dried.
- REFERENCE 4: 140:332648 Lys9 for Glu9 substitution in glucagon-like peptide-1(7-36) amide confers dipeptidylpeptidase IV resistance with cellular and metabolic actions similar to those of established antagonists glucagon-like peptide-1(9-36) amide and exendin (9-39). Green, B. D.; Mooney, M. H.; Gault, V. A.; Irwin, N.; Bailey, C. J.; Harriott, P.; Greer, B.; Flatt, P. R.; O'Harte, F. P. M. (School of Biomedical Sciences, University of Ulster, Coleraine, UK). Metabolism, Clinical and Experimental, 53(2), 252-259 (English) 2004. CODEN: METAAJ. ISSN: 0026-0495. Publisher: W. B. Saunders Co..
- The incretin hormone glucagon-like peptide-1(7-36)amide (GLP-1) has been AΒ deemed of considerable importance in the regulation of blood glucose. Its effects, mediated through the regulation of insulin, glucagon, and somatostatin, are glucose-dependent and contribute to the tight control of glucose levels. Much enthusiasm has been assigned to a possible role of GLP-1 in the treatment of type 2 diabetes. GLP-1's action unfortunately is limited through enzymic inactivation caused by dipeptidylpeptidase IV (DPP IV). It is now well established that modifying GLP-1 at the N-terminal amino acids, His7 and Ala8, can greatly improve resistance to this enzyme. Little research has assessed what effect Glu9-substitution has on GLP-1 activity and its degradation by DPP IV. Here, we report that the replacement of Glu9 of GLP-1 with Lys dramatically increased resistance to DPP IV. This analog, (Lys9)GLP-1, exhibited a preserved GLP-1 receptor affinity, but the usual stimulatory effects of GLP-1 were completely eliminated, a trait duplicated by the other established GLP-1-antagonists, exendin (9-39) and GLP-1(9-36) amide. We investigated the in vivo antagonistic actions of (Lys9)GLP-1 in comparison with GLP-1(9-36)amide and exendin (9-39) and revealed that this novel analog may serve as a functional antagonist of the GLP-1 receptor.
- REFERENCE 5: 140:123174 Insulin-producing cell compositions and related analysis and therapeutic methods. Kim, Seung; Rulifson, Ingrid; Hori, Yuichi (The Board of Trustees of the Leland Stanford Junior University, USA). PCT Int. Appl. WO 2004010933 A2 20040205, 61 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,

- VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US23346 20030725. PRIORITY: US 2002-PV398939 20020725; US 2002-PV426632 20021114.
- AB The disclosure relates, in part, to insulin-producing cell compns., methods for generating insulin-producing cell compns. by using a cell proliferation inhibitor, and therapeutic and non-therapeutic methods for using the insulin-producing cell compns.
- REFERENCE 6: 140:105831 Pharmaceutical compositions and uses of GLP-1 mimetics for the treatment of diabetes. Steiness, Eva (Zealand Pharma A/S, Den.). PCT Int. Appl. WO 2004005342 Al 20040115, 68 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-DK463 20030702. PRIORITY: US 2002-PV393917 20020704; US 2003-PV465613 20030424.
- AB The present invention relates to use of GLP-1 or a related mol. having GLP-effect for the manufacture of a medicament for preventing or treating diabetes in a mammal. The amount and timing of administration of said medicament are subsequently reduced to produce a 'drug holiday'. Practice of the invention achieves effective therapy without continuous drug exposure and without continuous presence of therapeutic levels of the drug. The invention also discloses a method of treating diabetes and related disorders in a mammal by administering glucagon like peptide (GLP-1) or a related mol. having GLP-1 like effect and thereby providing a therapeutically effective amount of endogenous insulin.
- REFERENCE 7: 140:28048 Palladium-mediated, site-specific cleavage and C-terminal amidation of peptides. Seo, Jin Seog; Holmquist, Barton; Strydom, Daniel (Restoragen Inc., USA). PCT Int. Appl. WO 2003099853 A2 20031204, 49 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US16648 20030523. PRIORITY: US 2002-PV383362 20020524.
- As ingle-step method of specific cleavage of a peptide near the C-terminus with concomitant palladium-mediated amidation of the newly-generated C-terminus is described for use in the processing of proteins manufactured by expression of the cloned gene in a suitable fermentation host. The reaction is directed to a specific peptide bond by placing it immediately N-terminal tripeptide. The tripeptide has an N-terminal cysteine, the second amino acid may be any, and the C-terminal peptide may be cysteine, histidine, or methionine.
- REFERENCE 8: 140:24699 Palladium-promoted hydrolytic cleavage of polypeptides in concentrated organic acid. Seo, Jin Seog; Strydom, Daniel; Holmquist, Barton (Restoragen Inc., USA). PCT Int. Appl. WO 2003100015 A2 20031204, 56 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,

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AB The invention provides a process for palladium-promoted hydrolytic cleavage of polypeptides at a Cys-His cleavage site in a reaction medium comprising a concentrated organic acid. In one embodiment, a chimeric protein comprised of a leader sequence joined by a Cys-His cleavage site to the N-terminus of the peptide is cleaved by solubilizing the chimeric protein in a reaction mixture comprised of a palladium promotor dissolved in a high-concentration organic acid solvent. Acetic acid, citric acid, lactic acid,

maleic acid, malonic acid, propionic acid, pyruvic acid, tartaric acid, and tricarballylic acid are preferred acids. These reaction media solubilize chimeric proteins or inclusion bodies previously considered to be relatively insol. and such solubilization, rather than decreasing the specificity of cleavage, actually leads to improved yields of cleaved peptide. Importantly, the process cleaves such chimeric proteins in a manner that facilitates addnl. processing necessary to post-translationally modify the cleaved peptide, e.g., amidation. The examples provided are to disclose techniques used in general, with specific uses illustrated for palladate promoted cleavages of T7tag-Vg-D4K-CH-GRF(1-44)-A (SEQ ID NO:2), T7tag-Vg-D4K-CH-GRF(1-44)-CH (SEQ ID NO: 1), T7tag-Vg-GsPR-CH-PTH(1-34) (SEQ ID NO:3), and T7tag-Vg-D4K-CH-PTH(1-84) (SEQ ID NO:4). The process of the instant invention provides a highly site-specific process for palladium-promoted hydrolytic cleavage of polypeptides under reaction conditions that are relatively insensitive to variations in reactant concentration, temperature or

process is conformationally and sequence-independent, i.e., it achieves high cleavage yield irresp. of the type of amino acid groups adjacent to the specified cleavage site. Further, the process of the instant invention cleaves polypeptides under conditions which limit the formation of unwanted side-products and which enable the use of chloride-containing catalysts and reaction-media.

REFERENCE 9: 139:272042 Glucose-dependent insulin-secreting cells transfected with human glucagon-like peptide-1 (GLP-1) for diabetes gene therapy. Perfetti, Riccardo; Hui, Hongxiang (Cedars-Sinai Medical Center, USA). PCT Int. Appl. WO 2003078462 A2 20030925, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US7210 20030311. PRIORITY: US 2002-97230 20020312.

AB Disclosed herein are cells that secrete insulin in a glucose-dependent manner. The cell line comprises insulin-secreting cells that have been transfected with a minigene construct comprising a nucleotide sequence encoding for glucagon-like peptide-1 (GLP-1). In preferred embodiments, the minigene construct is operatively associated with a promoter. The cell line may be used to treat diabetes or other conditions in which delivering insulin in a glucose-dependent manner would be advantageous, to investigate the function and development of pancreatic cells, and to test the efficacy of drugs that stimulate insulin secretion. The cells may be implanted in a mammal, or may be included in a device that resides

pH.

exterior to the mammal, yet which delivers insulin to the mammal in response to the glucose level of a body fluid in contact therewith. The minigene construct may also be implemented in conjunction with an in vivo gene transfer approach.

REFERENCE 10: 139:219381 Coupling proteins to a modified polysaccharide, especially oxidized hydroxyethyl starch for use as drugs. Hemberger, Juergen; Orlando, Michele (Biotechnologie - Gesellschaft Mittelhessen MbH, Germany). PCT Int. Appl. WO 2003074087 Al 20030912, 38 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (German). CODEN: PIXXD2. APPLICATION: WO 2003-EP2083 20030228. PRIORITY: DE 2002-10209821 20020306.

The invention relates to a method for coupling proteins to a AΒ starch-derived modified polysaccharide. The binding interaction between the modified polysaccharide and the protein is based on a covalent bond which is the result of a coupling reaction between the terminal aldehyde group or a functional group of the modified polysaccharide mol. resulting from the chemical reaction of this aldehyde group and a functional group of the protein which reacts with the aldehyde group or with the resulting functional group of the polysaccharide mol. The bond directly resulting from the coupling reaction can be optionally modified by a further reaction to the aforementioned covalent bond. The invention further relates to pharmaceutical compns. that comprise conjugates formed in this coupling process and to the use of said conjugates and compns. for the prophylaxis or therapy of the human or animal body. Thus high (130 kD) and low mol. weight (10 kD) hydroxyethyl starch was selectively oxidized and coupled to various proteins, e.g. human serum albumin, myoglobin, superoxide dismutase, streptokinase, asparaginase.

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E1
                   DIOXO-1H-PYRROL-1-YL)-1-OXOPROPYL)-L-LYSINAMIDE)-/CN
                   EXENDIN 3 (HELODERMA HORRIDUM), 39A-(N6-(3-(2,5-DIHYDRO-2,5-
E2
                   DIOXO-1H-PYRROL-1-YL)-1-OXOPROPYL)-L-LYSINAMIDE)-, PENTAKIS(
                   TRIFLUOROACETATE) (SALT)/CN
             1 --> EXENDIN 4/CN
E3
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CN Exendin 4 (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Extendin-4
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LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CANCERLIT,
CAPLUS, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IPA, MEDLINE, MRCK*,
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PHAR, PROMT, PROUSDDR, RTECS\*, TOXCENTER, USPATFULL (\*File contains numerically searchable property data) DT.CA CAplus document type: Conference; Journal; Patent Roles from patents: ANST (Analytical study); BIOL (Biological study); RL.P PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses) Roles for non-specific derivatives from patents: BIOL (Biological RLD, P study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses) Roles from non-patents: BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses) RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses) \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\* 181 REFERENCES IN FILE CA (1907 TO DATE) 21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA 182 REFERENCES IN FILE CAPLUS (1907 TO DATE) REFERENCE 1: 140:400707 2: 140:400441 REFERENCE 3: 140:386447 REFERENCE 4: 140:386159 REFERENCE 5: 140:368703 REFERENCE REFERENCE 6: 140:363055 REFERENCE 7: 140:363054 REFERENCE 8: 140:363053 REFERENCE 9: 140:334648 REFERENCE 10: 140:332648 => s 15 not 16 1 L5 NOT L6 => e hgeqtftsdlskqmeeeavrlfiewlkngg/sqsp 'SQSP' IS NOT A VALID EXPAND FIELD CODE FOR FILE 'REGISTRY' The indicated field code is not available for EXPAND in this file. To see a list of valid EXPAND field codes, enter HELP SFIELDS at an arrow prompt (=>). => s hgegtftsdlskgmeeeavrlfiewlkngg/sgsp 147 HGEGTFTSDLSKQMEEEAVRLFIEWLKNGG/SQSP => s h..qtfitsdlskqmeeeavrlfiewlknggpssgappps/sqsp 3 H..GTF'ITSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS/SQSP => s dlskgmeeeavrlfiewlknggpssgappps/sgsp 117 DLSKOMEEEAVRLFIEWLKNGGPSSGAPPPS/SQSP => fil medl, hcap, biosis, embase; s 110 or 19 or 19 or 12 or 16 or 14 COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

116.22 116.43 FULL ESTIMATED COST SINCE FILE DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) TOTAL ENTRY SESSION -1.32 -1.32 CA SUBSCRIBER PRICE FILE 'MEDLINE' ENTERED AT 15:50:52 ON 16 JUN 2004 FILE 'HCAPLUS' ENTERED AT 15:50:52 ON 16 JUN 2004 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS) FILE 'BIOSIS' ENTERED AT 15:50:52 ON 16 JUN 2004 COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R) FILE 'EMBASE' ENTERED AT 15:50:52 ON 16 JUN 2004 COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved. 127 FILE MEDLINE 277 FILE HCAPLUS L12 L13 243 FILE BIOSIS 24 FILE EMBASE L14 TOTAL FOR ALL FILES 671 L10 OR L9 OR L9 OR L2 OR L6 OR L4 => s 115 and (insulin or non insulin or diabet?) 74 FILE MEDLINE 200 FILE HCAPLUS L17 144 FILE BIOSIS L18 L19 18 FILE EMBASE TOTAL FOR ALL FILES

436 L15 AND (INSULIN OR NON INSULIN OR DIABET?)

=> s 120 and (pharm?(5a) (vehicle or carrier) UNMATCHED LEFT PARENTHESIS 'AND (PHARM?' The number of right parentheses in a query must be equal to the number of left parentheses.

=> s 120 and (pharm?(5a) (vehicle or carrier)) L21 O FILE MEDLINE L22 1 FILE HCAPLUS

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TOTAL FOR ALL FILES

1 L20 AND (PHARM? (5A) (VEHICLE OR CARRIER))

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L25 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

2003:334829 HCAPLUS ΑN

138:343889

Novel pharmaceutical compounds containing drugs bound to polypeptides TI

Picariello, Thomas

New River Pharmaceuticals Inc., USA

PCT Int. Appl., 4662 pp.

CODEN: PIXXD2

DTPatent

LA English FAN.CNT 1 APPLICATION NO. DATE PATENT NO. KIND DATE \_\_\_\_\_\_ \_\_\_\_\_\_ WO 2003034980 A2 20030501 WO 2003034980 C1 20031120 WO 2001-US43089 20011114 ΡI W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG A1 20040331 EP 2001-274606 20011114 EP 1401374 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-274622P P 20001114
WO 2001-US43089 W 20011114 Compns. comprising polypeptides and drugs covalently attached to the AΒ polypeptide are disclosed. Also provided is a method for delivery of these drugs to a patient comprising administering to the patient a composition comprising a polypeptide and a drug covalently attached to the polypeptide. Also provided is a method for protecting drugs from degradation comprising covalently attaching them to a polypeptide. Also provided is a method for controlling release of drugs from a composition comprising covalently attaching them to the polypeptide. => s knudsen ?/au or knudsen, ?/au 2471 FILE MEDLINE L26 L27 2396 FILE HCAPLUS L28 2905 FILE BIOSIS L29 1837 FILE EMBASE TOTAL FOR ALL FILES 9609 KNUDSEN ?/AU OR KNUDSEN, ?/AU => s 130 and (110 or 19 or 18 or 12 or 14 or 16) 1 FILE MEDLINE L31 L32 9 FILE HCAPLUS L33 4 FILE BIOSIS L34 O FILE EMBASE TOTAL FOR ALL FILES 14 L30 AND (L10 OR L9 OR L8 OR L2 OR L4 OR L6) => dup rem 135 PROCESSING COMPLETED FOR L35 13 DUP REM L35 (1 DUPLICATE REMOVED) => d 1-13 cbib abs L36 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN 2004:354975 Document No. 140:386038 Stabilized exendin-4 compounds, their preparation, and their therapeutic use. Ebbehoj, Kirsten; Jepsen, Trine; Knudsen, Carsten Boye; Larsen, Bjarne Due; Knott, David (Zealand Pharma A/S, Den.). PCT Int. Appl. WO 2004035623 A2 20040429, 59 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,

- LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-DK651 20031002. PRIORITY: US 2002-PV415626 20021002.
- AB The invention discloses compns. comprising a stabilized Exendin-4 (1-39) and related compds. The invention describes stabilized Exendin-4 agonists that include at least one modified amino acid residue particularly at positions Gln 13, Met14, Trp25, or Asn28 of the Exendin-4 (1-39) mol. Disclosed are preferred modifications of deaminated, hydrolyzed, oxidized, or isomerized reaction products of the specified amino acid residues corresponding to the same positions in the Exendin-4 mol. The invention also relates to methods of making and using the stabilized Exendin compds., such as for the treatment of diabetes.
- L36 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN Document No. 139:302514 Methods and composition for the 2003:818306 treatment of cardiovascular diseases using GLP-1 analogs to reduced the levels of brain natriuretic peptide (BNP). Knudsen, Liselotte Bjerre; Rolin, Bida Charlotte; Carr, Richard David; Selmer, Johan; Larsen, Jens; Elbrond, Bodil; Nielsen, Lars Bo; Christoffersen, Christina (Novo Nordisk A/S, Den.). PCT Int. Appl. WO 2003084563 A1 20031016, 28 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-DK216 20030402. PRIORITY: DK 2002-499 20020404; US 2002-PV375255 20020423.
- AB Methods and uses for the treatment and prevention of cardiac and cardiovascular diseases comprising administration of a GLP-1 agonist to reduce brain natriuretic peptide (BNP) levels in plasma and/or heart tissue. The treatment can be combined with other therapies such as anti-diabetic, anti-obesity, lipid modulation, anti-hypertensive and anti-osteoporosis therapies.
- L36 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

  2003:633497 Document No. 139:174286 Use of GLP-1 compound for treatment of critically ill patients. Knudsen, Lotte Bjerre; Selmer, Johan;

  Hansen, Kristian Tage (Novo Nordisk A/S, Den.). PCT Int. Appl. WO

  2003066084 A1 20030814, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-DK61 20030131. PRIORITY: DK 2002-184 20020207.
- AB Use of medicament for life saving treatment of critically ill patients SIRS patients, and method of treatment. The medicament comprises a GLP-1 compound which effectively controls the blood glucose level.
- L36 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN 2003:570838 Document No. 139:128032 Combined use of a GLP-1 compound and another drug for treating dyslipidemia. Knudsen, Lotte Bjerre;

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Selmer, Johan (Novo Nordisk A/S, Den.). PCT Int. Appl. WO 2003059378 A2 20030724, 20 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-DK887 20021220. PRIORITY: DK 2001-1970 20011229; DK 2002-759 20020517.
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- AB Methods and uses for treatment of dyslipidemia comprising administration of a GLP-1 compound and another antidyslipidemic drug.
- L36 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

  2003:570833 Document No. 139:111682 Combined use of a GLP-1 compound and a modulator of diabetic late complications. Knudsen, Lotte Bjerre; Selmer, Johan (Novo Nordisk A/S, Den.). PCT Int. Appl. WO 2003059372 A2 20030724, 22 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-DK888 20021220. PRIORITY: DK 2001-1969 20011229; DK 2002-760 20020517.
- AB Methods and uses for treatment of diabetic late complications comprising administration of a GLP-1 compound and a modulator of diabetic complications.
- L36 ANSWER 6 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2003:460286 Document No.: PREV200300460286. Central administration of oxyntomodulin inhibits food intake without causing a conditioned taste aversion. Lykkegaard, Kirsten [Reprint Author]; Knudsen, Sanne; Vrang, Niels; Larsen, Philip; Tang-Christensen, Mads. Roedovre, Denmark. Diabetes, (2003) Vol. 52, No. Supplement 1, pp. A348. print. Meeting Info.: 63rd Scientific Sessions of the American Diabetes Association. New Orleans, LA, USA. June 13-17, 2003. American Diabetes Association. ISSN: 0012-1797 (ISSN print). Language: English.
- L36 ANSWER 7 OF 13 MEDLINE on STN DUPLICATE 1
  2002458853. PubMed ID: 12217892. The long-acting GLP-1 derivative NN2211
  ameliorates glycemia and increases beta-cell mass in diabetic mice. Rolin
  Bidda; Larsen Marianne O; Gotfredsen Carsten F; Deacon Carolyn F; Carr
  Richard D; Wilken Michael; Knudsen Lotte Bjerre. (Novo Nordisk,
  DK-2880 Bagsvaerd, Denmark.. bidr@novonordisk.com). American journal of
  physiology. Endocrinology and metabolism, (2002 Oct) 283 (4) E745-52.
  Journal code: 100901226. ISSN: 0193-1849. Pub. country: United States.
  Language: English.
- AB NN2211 is a long-acting, metabolically stable glucagon-like peptide-1 (GLP-1) derivative designed for once daily administration in humans. NN2211 dose dependently reduced the glycemic levels in ob/ob mice, with antihyperglycemic activity still evident 24 h postdose. Apart from an initial reduction in food intake, there were no significant differences between NN2211 and vehicle treatment, and body weight was not affected. Histological examination revealed that beta-cell proliferation and mass were not increased significantly in ob/ob mice with NN2211, although there was a strong tendency for increased proliferation. In db/db mice, exendin-4 and NN2211 decreased blood glucose compared with vehicle, but

NN2211 had a longer duration of action. Food intake was lowered only on day 1 with both compounds, and body weight was unaffected. beta-Cell proliferation rate and mass were significantly increased with NN2211, but with exendin-4, only the beta-cell proliferation rate was significantly increased. In conclusion, NN2211 reduced blood glucose after acute and chronic treatment in ob/ob and db/db mice and was associated with increased beta-cell mass and proliferation in db/db mice. NN2211 is currently in phase 2 clinical development.

- L36 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

  2001:676621 Document No. 135:237105 Lowering serum lipids by administering a GLP-1 agonist. Knudsen, Liselotte Bjerre; Selmer, Johan; Sturis, Jeppe; Larsen, Philip Just (Novo Nordisk A/S, Den.). PCT Int. Appl. Wo 2001066135 A1 20010913, 52 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-DK150 20010308. PRIORITY: DK 2000-375 20000308.
- The present invention relates to a method for lowering serum lipids, e.g.. triglycerides and/or cholesterol in a subject comprising administering a GLP-1 agonist to said subject. The specifically claimed GLP-1 agonists are Arg26, Lys34 [N- $\epsilon$ -[ $\gamma$ -Glu(N- $\alpha$ -hexadecanoyl)]]-GLP-1(7-37), Arg34, Lys26 [N- $\epsilon$ -[ $\gamma$ -Glu(N- $\alpha$ -hexadecanoyl)]]-GLP-1(7-37), exendin-3, exendin-4, Val8-GLP-1(7-37), Thr8-GLP-1(7-37), Met8-GLP-1(7-37), and Gly8-GLP-1(7-37).
- L36 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

  2001:380424 Document No. 134:361831 GLP-1 agonists, exendin analogs, or GLP-1 receptor-binding non-peptide for use in inhibition of pancreatic beta cell degeneration. Knudsen, Liselotte Bjerre; Godtfredsen, Carsten Foged; Petersen, Jacob Sten; Carr, Richard David (Novo Nordisk A/S, Den.). PCT Int. Appl. WO 2001035988 A1 20010525, 59 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-DK625 20001110. PRIORITY: DK 1999-1628 19991112; DK 2000-270 20000222.
- This invention relates to a method for modulating, inhibiting or decreasing or preventing beta cell degeneration, loss of beta cell function, beta cell dysfunction, and/or death of beta cells, such as necrosis or apoptosis of beta cells in a subject comprising administering a GLP-1 agonist to said subject. The GLP-1 agonist is selected from a GLP-1 analog, a GLP-1 derivative, exendin, exendin analogs or derivs., or a non-peptide which binds to a GLP-1 receptor with an affinity constant (KD) below 1  $\mu M$ . Specifically claimed is the GLP-1 derivative Arg34,Lys26(N- $\epsilon$ ( $\gamma$ -Glu(N- $\alpha$ -hexadecanoyl)))-GLP-1(7-37).
- L36 ANSWER 10 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2001:448984 Document No.: PREV200100448984. NN2211, a GLP-1 derivative, has a long lasting blood glucose lowering effect in db/db mice: A comparison with exendin-4. Larsen, Marianne O. [Reprint author]; Rolin, Bidda [Reprint author]; Wilken, Michael [Reprint author]; Carr, Richard D. [Reprint author]; Knudsen, Lotte Bjerre [Reprint author].

Bagsvaerd, Denmark. Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A312. print.

Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001. American Diabetes Association.

CODEN: DIAEAZ. ISSN: 0012-1797. Language: English.

CODEN: DBTGAJ. ISSN: 0012-186X. Language: English.

L36 ANSWER 11 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2002:568785 Document No.: PREV200200568785. NN2211, a long-acting GLP-1 derivative, decreases blood glucose and stimulates beta-cell proliferation in DB/DB mice. Larsen, M. O. [Reprint author]; Gotfredsen, C. F. [Reprint author]; Rolin, B. [Reprint author]; Wilken, M. [Reprint author]; Knudsen, L. Bjerre [Reprint author]. Novo Nordisk A/S, Bagsvaerd, Denmark. Diabetologia, (August, 2001) Vol. 44, No. Supplement 1, pp. A197. print.

Meeting Info.: 37th Annual Meeting of the European Association for the Study of Diabetes. Glasgow, Scotland, UK. September 09-13, 2001. European Association for the Study of Diabetes.

L36 ANSWER 12 OF 13 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN 2001:441487 Document No.: PREV200100441487. Effects of NN2211, a long acting derivative of GLP-1, on beta-cell proliferation and beta-cell mass in db/db mice. Gotfredsen, Carsten F. [Reprint author]; Larsen, Marianne O. [Reprint author]; Knudsen, Lotte Bjerre [Reprint author]. Bagsvaerd, Denmark. Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A31. print.

Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001. American Diabetes Association.

L36 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2004 ACS on STN

CODEN: DIAEAZ. ISSN: 0012-1797. Language: English.

1999:566077 Document No. 131:194808 GLP-1 derivatives of GLP-1 and exendin with a protracted profile of action. Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Madsen, Kjeld (Novo Nordisk A/s, Den.). PCT Int. Appl. WO 9943708 A1 19990902, 70 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-DK86 19990225. PRIORITY: DK 1998-274 19980227; US 1998-PV84357 19980505.

AB The present invention relates to derivs. exendin and of GLP-1(7-C), wherein C is 35 or 36, which derivs. have just one lipophilic substituent which is attached to the C-terminal amino acid residue. The derivs. have a protracted action relative to GLP-1(7-37) and are useful for treating insulin-dependent and noninsulin-dependent diabetes mellitus. The derivs. of the invention can be combined with other antidiabetics or oral hypoglycemic agents. Pharmaceutical formulations containing the derivs. of the invention are also claimed.

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589 HEXADECANOYL

239 EXENDIN?

L1 0 AMINOBUTYROYL(L)HEXADECANOYL(L)EXENDIN?

=> s aminobuty?(1)hexadecanoy1(1)exendin?

12081 AMINOBUTY?

589 HEXADECANOYL

239 EXENDIN?

L2 0 AMINOBUTY? (L) HEXADECANOYL (L) EXENDIN?

=> s aminobuty?(1)hexadecanoyl?

12081 AMINOBUTY?

589 HEXADECANOYL?

L3 0 AMINOBUTY? (L) HEXADECANOYL?

=> e "exendin-4-(7-45)-nh2"/cn

E1 1 EXENDIN-4 FUSION PROTEIN WITH LINKER AND HUMAN SERUM ALBUMIN /CN

E2 1 EXENDIN-4 WITH A C-TERMINAL EXTENSION FUSION PROTEIN WITH HU

MAN IGG1 FRAGMENT/CN
E3 0 --> EXENDIN-4-(7-45)-NH2/CN

E4 1 FXEPANOL/CN

E5 1 EXESTROL/CN

E6 1 EXF/CN

E7 1 EXF 01/CN

E8 1 EXF 37/CN E9 1 EXF 51/CN

E9 1 EXF 51/CN E10 1 EXFOLIAC/CN

E11 1 EXFOLIAC 10/CN

E12 1 EXFOLIAC 15/CN

=> e "exendin-4"/cn

```
EXENDIN(9-39) AMIDE/CN
Ei
            1
                 EXENDIN-3 (HELODERMA HORRIDUM)/CN
            1
E2
            0 --> EXENDIN-4/CN
EЗ
                EXENDIN-4 (HELODERMA SUSPECTUM)/CN
             1
\cdot E 4
                  EXENDIN-4 FUSION PROTEIN WITH A LINKER AND HUMAN IGG1 FRAGME
            1
E5
                   NT/CN
                  EXENDIN-4 FUSION PROTEIN WITH HUMAN IGG1 FRAGMENT/CN
Ε6
            1
                EXENDIN-4 FUSION PROTEIN WITH HUMAN SERUM ALBUMIN/CN EXENDIN-4 FUSION PROTEIN WITH LINKER AND HUMAN SERUM ALBUMIN
             1
E7
             1
E8
                   /CN
Ε9
            1
                  EXENDIN-4 WITH A C-TERMINAL EXTENSION FUSION PROTEIN WITH HU
                  MAN IGG1 FRAGMENT/CN
                  EXEPANOL/CN
             1
E10
             1
                  EXESTROL/CN
E11
                  EXF/CN
             1
E12
=> fil medl, hcap, biosis, embase, wpids, uspatful; s amino(1) butyroyl(1) hexadecanoyl?
                                                  SINCE FILE TOTAL
COST IN U.S. DOLLARS
                                                       ENTRY
                                                               SESSION
                                                       37.12
                                                                37.75
FULL ESTIMATED COST
FILE 'MEDLINE' ENTERED AT 16:01:10 ON 16 JUN 2004
FILE 'HCAPLUS' ENTERED AT 16:01:10 ON 16 JUN 2004
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CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
             O FILE MEDLINE
L4
             O FILE HCAPLUS
L_5
             0 FILE BIOSIS
L6
L7
             O FILE EMBASE
             O FILE WPIDS
L8
            18 FILE USPATFULL
TOTAL FOR ALL FILES
           18 AMINO(L) BUTYROYL(L) HEXADECANOYL?
\Rightarrow s 110 (1) exendin?
L11 0 FILE MEDLINE
             O FILE HCAPLUS
L12
             0 FILE BIOSIS
L13
L14
             O FILE EMBASE
             O FILE WPIDS
L15
             O FILE USPATFULL
TOTAL FOR ALL FILES
L17 0 L10 (L) EXENDIN?
```

=> d 110 1-18 L10 ANSWER 1 OF 18 USPATFULL on STN 2004:121040 USPATFULL ANGamma-hydroxybutyrate compositions containing carbohydrate, lipid or TIamino acid carriers Mamelak, Mortimer, Toronto, CANADA IN Houghton, William C., St. Paul, MN, UNITED STATES Reardan, Dayton T., Excelsior, MN, UNITED STATES Miller, Brian L., EdenPraine, MN, UNITED STATES 20040513 PΙ US 2004092455 Α1 US 2003-381224 ΑI A120031103 (10) WO 2001-US29569 20010921 DT Utility APPLICATION LN.CNT 942 INCLM: 514/023.000 INCL INCLS: 514/057.000; 536/066.000; 536/116.000 NCLM: 514/023.000 NCL NCLS: 514/057.000; 536/066.000; 536/116.000 IC [7] ICM: A61K031-716 ICS: A61K031-70; C08B013-00; C07H015-04 CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 2 OF 18 USPATFULL on STN 2003:78377 USPATFULL AN Silver halide photographic lightsensitive material and image forming TΙ method using the same Hosokawa, Junichiro, Minami-Ashigara-shi, JAPAN IN A1 20030320 PΙ US 2003054297 US 6727050 B2 20040427 US 2002-108956 A1 20020329 (10) ΑТ PRAI JP 2001-97245 20010329 DTUtility FS APPLICATION LN.CNT 4281 INCLM: 430/350.000 INCL INCLS: 430/567.000; 430/566.000; 430/523.000; 430/617.000 NCL NCLM: 430/351.000 IC [7] ICM: G03C001-32 ICS: G03C001-42; G03C001-498; G03C001-91 CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 3 OF 18 USPATFULL on STN 2002:191440 USPATFULL AN Silver halide color photographic light-sensitive material TΙ Koide, Tomoyuki, Minami-ashigara-shi, JAPAN ΤN Kawagishi, Toshio, Minami-ashigara-shi, JAPAN US 2002102504 Α1 20020801 PT US 6528243 В2 20030304 A1 20011025 (9) US 2001-983805 ΑT 20001027 JP 2000-329527 PRAI DT Utility FS APPLICATION LN.CNT 3426 INCLM: 430/543.000 TNCL INCLS: 430/567.000; 430/619.000; 430/350.000; 430/603.000; 430/600.000 NCL. 430/543.000

430/206.000; 430/351.000; 430/376.000; 430/471.000; 430/550.000;

430/567.000; 430/600.000; 430/601.000; 430/603.000

```
ΙC
        [7]
       ICM: G03C001-035
       ICS: G03C001-09; G03C001-42; G03C001-498
·CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L10 ANSWER 4 OF 18 USPATFULL on STN
       2002:164631 USPATFULL
AN
       Method of processing silver halide color photographic lightsensitive
TI
       material
       Kikuchi, Makoto, Minami-Ashigara-shi, JAPAN
ΙN
       Ishii, Yoshio, Minami-Ashigara-shi, JAPAN
       Kawagishi, Toshio, Minami-Ashigara-shi, JAPAN
                                20020704
       US 2002086249
                          A1
PΙ
       US 6432624
                           В2
                                20020813
       US 2001-846397
                                20010502 (9)
                           Α1
ΑI
                           20000508
       JP 2000-134730
PRAI
       JP 2000-172788
                           20000608
DT
       Utility
       APPLICATION
FS
LN.CNT 5356
       INCLM: 430/380.000
INCL
       INCLS: 430/390.000; 430/391.000; 430/440.000; 430/442.000; 430/567.000;
               430/572.000
               430/405.000
NCL
       NCLM:
       NCLS: 430/448.000
ΙC
       [7]
       ICM: G03C007-413
       ICS: G03C005-30; G03C001-12; G03C001-035; G03C001-42
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L10 ANSWER 5 OF 18 USPATFULL on STN
       2002:105865 USPATFULL
ΑN
TΙ
       Silver halide photographic light-sensitive material and method of
       forming image therein
ΙN
       Uchida, Minoru, Minami-Ashigara-shi, JAPAN
       FUJI PHOTO FILM CO., LTD. (non-U.S. corporation)
PΑ
       US 2002055070
PΙ
                          A1
                                20020509
       US 6686141
                           В2
                                20040203
       US 2001-875902
                          A1
                                20010608 (9)
ΑI
                           20000608
PRAI
       JP 2000-172800
DT
       Utility
FS
       APPLICATION
LN.CNT 4523
INCL
       INCLM: 430/375.000
       INCLS: 430/566.000; 430/567.000; 430/572.000; 430/390.000
       NCLM: 430/567.000
NCLS: 430/569.000
NCL
       [7]
TC
       ICM: G03C001-035
       ICS: G03C001-10; G03C001-42; G03C005-29
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 6 OF 18 USPATFULL on STN
       2002:54570 USPATFULL
ΑN
       Method of processing silver halide color photographic light-sensitive
TΙ
       Hosokawa, Junichiro, Minami-Ashigara-shi, JAPAN
ΙN
PΙ
       US 2002031731 A1
                                20020314
       US 6555299
                          В2
                                20030429
       US 2001-876138
                          A1
                                20010608 (9)
AΙ
PRAI
       JP 2000-173607
                           20000609
       Utility
```

FŚ APPLICATION LN.CNT 5448 .INCL INCLM: 430/380.000 INCLS: 430/567.000; 430/603.000; 430/506.000; 430/505.000; 430/566.000; 430/383.000 430/351.000 NCL NCLM: TC [7] ICM: G03C001-035 ICS: G03C007-32; G03C001-42; G03C001-09 CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 7 OF 18 USPATFULL on STN 2000:167716 USPATFULL ΑN Color-image forming method using a silver halide color photographic ΤT light-sensitive material IN Makuta, Toshiyuki, Minami-ashigara, Japan PΑ Fuji Photo Film Co., Ltd., Kanagawa-Ken, Japan (non-U.S. corporation) US 6159668 20001212 PΙ US 2000-478548 20000106 (9) AΙ Division of Ser. No. US 1999-262855, filed on 4 Mar 1999 RLI JP 1998-71220 19980306 PRAI JP 1998-71221 19980306 JP 1998-101886 19980331 DT Utility FS Granted LN.CNT 4718 INCL INCLM: 430/373.000 INCLS: 430/405.000; 430/414.000; 430/415.000; 430/943.000 NCL NCLM: 430/373.000 NCLS: 430/405.000; 430/414.000; 430/415.000; 430/943.000 IC [7] ICM: G03C007-407 430/373; 430/405; 430/414; 430/415; 430/943 CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 8 OF 18 USPATFULL on STN 2000:57520 USPATFULL AN TIColor-image forming method using a silver halide color photographic light-sensitive material ΙN Makuta, Toshiyuki, Minami-ashigara, Japan PA Fuji Photo Film Co., Ltd., Kanagawa-ken, Japan (non-U.S. corporation) PΙ US 6060225 20000509 ΑI US 1999-262855 19990304 (9) PRAI JP 1998-71220 19980306 JP 1998-71221 19980306 JP 1998-101886 19980331 DT Utility FS Granted LN.CNT 4011 INCLM: 430/405.000 INCL INCLS: 430/414.000; 430/415.000; 430/566.000; 430/943.000 NCL NCLM: 430/405.000 NCLS: 430/414.000; 430/415.000; 430/566.000; 430/943.000 IC [7] ICM: G03C007-413 EXF 430/405; 430/414; 430/415; 430/566; 430/943; 396/604; 396/609; 396/627 CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 9 OF 18 USPATFULL on STN ΑN 95:94902 USPATFULL TISpicamycin derivatives and their use as anticancer agents IN Otake, Noboru, Toshima, Japan

```
Kawai, Hiroyuki, Takasaki, Japan
       Kawasaki, Tomiko, Takasaki, Japan
       Odagawa, Atsuo, Takasaki, Japan
       Kamishohara, Masaru, Takasaki, Japan
       Sakai, Teruyuki, Takasaki, Japan
       Kirin Beer Kabushiki Kaisha, Tokyo, Japan (non-U.S. corporation)
PΑ
PΙ
                                 19951024
       US 5461036
                                 19920708 (7)
       US 1992-910640
ΑI
       JP 1991-198903
                            19910712
PRAI
       JP 1991-326845
                            19911115
       JP 1992-110665
                            19920403
DT
       Utility
FS
       Granted
LN.CNT 5193
       INCLM: 514/046.000
INCL
       INCLS: 536/027.600
               514/046.000
NCL
       NCLM:
       NCLS: 536/027.600
IC
       [6]
       ICM: A61K031-70
       ICS: C07H019-16
       536/29.11; 536/27.6; 514/45; 514/46
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L10 ANSWER 10 OF 18 USPATFULL on STN
       94:15801 USPATFULL
ΑN
ΤI
       Process for the preparation of stabilized styrene copolymers containing
       elastomer particles
       Gilg, Bernard, St. Louis-La-Chaussee, France
ΙN
       Rytz, Gerhard, Schwarzenburg, Switzerland
       Stauffer, Werner, Fribourg, Switzerland Clauss, Margot, Riedisheim, France
PΑ
       Ciba-Geigy Corporation, Ardsley, NY, United States (U.S. corporation)
       US 5288777
PΙ
                                19940222
ΑI
       US 1992-973478
                                19921109 (7)
       Division of Ser. No. US 1991-769916, filed on 30 Sep 1991, now patented,
RLI
       Pat. No. US 5194465, issued on 16 Mar 1993
PRAI
       CH 1990-3200
                            19901004
DT
       Utility
FS
       Granted
LN.CNT 915
       INCLM: 524/099.000
INCL
       INCLS: 524/087.000; 525/073.000; 525/203.000; 525/279.000
              524/099.000
       NCLM:
       NCLS: 524/087.000; 525/073.000; 525/203.000; 525/279.000
       [5]
       ICM: C08K005-3432
       ICS: C08K005-3415; C08G063-91; C08L039-04
       524/87; 524/99; 524/94; 525/203; 525/279; 525/73
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 11 OF 18 USPATFULL on STN
AN
       93:20561 USPATFULL
TΙ
       Stabilized styrene copolymers containing elastomer particles modified
       with a hindered amine
       Gilg, Bernard, St. Louis-la-Chaussee, France Rytz, Gerhard, Schwarzenburg, Switzerland
ΙN
       Stauffer, Werner, Fribourg, Switzerland
       Clauss, Margot, Riedisheim, France
PΑ
       Ciba-Geigy Corporation, Ardsley, NY, United States (U.S. corporation)
PΙ
       US 5194465
                                 19930316
AΙ
       US 1991-769916
                                19910930 (7)
```

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PRAI
       CH 1990-3200
                           19901004
DT
       Utility
FS
       Granted
LN.CNT 921
       INCLM: 524/099.000
INCL
       INCLS: 524/086.000; 524/094.000; 524/126.000; 524/128.000; 525/203.000;
              525/279.000; 546/184.000
NCL
       NCLM:
              524/099.000
              524/086.000; 524/094.000; 524/126.000; 524/128.000; 525/203.000;
       NCLS:
              525/279.000; 546/184.000
ΙC
       [5]
       ICM: C08K005-3415
       ICS: C08K005-3432; C08L039-04
       525/279; 525/203; 524/99; 524/94
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L10 ANSWER 12 OF 18 USPATFULL on STN
ΑN
       92:68151 USPATFULL
TΙ
       Heat-developable color photographic materials with combination of
       electron transfer agent and precursor
       Taguchi, Toshiki, Kanagawa, Japan
TN
       Nakamine, Takeshi, Kanagawa, Japan
       Kawata, Ken, Kanagawa, Japan
       Hirai, Hiroyuki, Kanagawa, Japan
       Fuji Photo Film Co., Ltd., Kanagawa, Japan (non-U.S. corporation)
PΑ
       US 5139919
                               19920818
PΙ
       US 1991-657937
                               19910221 (7)
AΙ
       Continuation of Ser. No. US 1988-275198, filed on 23 Nov 1988, now
RLI
       abandoned
       JP 1987-298571
                           19871126
PRAI
DT
       Utility
FS
       Granted
LN.CNT 1803
INCL
       INCLM: 430/203.000
       INCLS: 430/218.000; 430/223.000; 430/436.000; 430/443.000; 430/566.000;
              430/959.000; 430/351.000
NCL
       NCLM:
             430/203.000
              430/218.000; 430/223.000; 430/351.000; 430/436.000; 430/443.000;
       NCLS:
              430/566.000; 430/959.000
IC
       [5]
       ICM: G03C005-54
       ICS: G03C001-42
       430/203; 430/218; 430/223; 430/436; 430/438; 430/443; 430/959; 430/566;
EXF
       430/351
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L10 ANSWER 13 OF 18 USPATFULL on STN
       91:104086 USPATFULL
ΝA
ΤT
       Silver halide photographic material
ΤN
       Watanabe, Hiroyuki, Kanagawa, Japan
       Koya, Keizo, Kanagawa, Japan
       Yoshioka, Yasuhiro, Kanagawa, Japan
       Nakamura, Koki, Kanagawa, Japan
       Fuji Photo Film Co., Ltd., Kanagawa, Japan (non-U.S. corporation)
PΑ
PΙ
       US 5075208
                               19911224
       US 1990-581252
                               19900911 (7)
ΑТ
RLI
       Continuation of Ser. No. US 1988-285990, filed on 19 Dec 1988, now
       abandoned
PRAI
       JP 1987-320771
                          19871218
DT
       Utility
FS
       Granted
LN.CNT 3964
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INCL INCLM: 430/559.000 INCLS: 430/223.000; 430/564.000; 430/955.000; 430/957.000; 430/958.000; 430/959.000 NCL NCLM: 430/559.000 430/223.000; 430/564.000; 430/955.000; 430/957.000; 430/958.000; NCLS: 430/959.000 IC [5] ICM: G03C001-06 430/223; 430/564; 430/955; 430/956; 430/957; 430/958; 430/959 EXF CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 14 OF 18 USPATFULL on STN 90:85535 USPATFULL ΝA Heat developable color light-sensitive material TΙ Nakamura, Koki, Kanagawa, Japan ΙN Hirai, Hiroyuki, Kanagawa, Japan PΑ Fuji Photo Film Co., Ltd., Kanagawa, Japan (non-U.S. corporation) US 4968598 PΙ 19901106 US 1989-328394 ΑI 19890324 (7) JP 1988-70352 19880324 PRAI DT Utility FS Granted LN.CNT 1563 INCLM: 430/617.000 INCL INCLS: 430/214.000; 430/619.000 NCL NCLM: 430/617.000 NCLS: 430/203.000; 430/214.000; 430/216.000; 430/218.000; 430/619.000 [5] TC ICM: G03C001-06 430/214; 430/617; 430/619 EXF CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 15 OF 18 USPATFULL on STN 86:34205 USPATFULL ΑN TΙ Color image forming process comprising blocked magenta dye forming coupler Furutachi, Nobuo, Kanagawa, Japan ΙN Yoshida, Yoshinobu, Kanagawa, Japan Fuji Photo Film Co., Ltd., Kanagawa, Japan (non-U.S. corporation) PΑ US 4594313 19860610 PΙ ΑI US 1985-710891 19850312 (6) JP 1984-46874 19840312 PRAI Utility DT Granted FS LN.CNT 1236 INCL INCLM: 430/381.000 INCLS: 430/387.000; 430/553.000; 430/555.000; 430/557.000; 430/558.000; 430/955.000 NCLM: 430/381.000 NCL NCLS: 430/387.000; 430/553.000; 430/555.000; 430/557.000; 430/558.000; 430/955.000 IC [4] ICM: G03C007-00 ICS: G03C001-08; G03C007-16; G03C007-32 430/553; 430/555; 430/557; 430/558; 430/955; 430/387; 430/381 EXF CAS INDEXING IS AVAILABLE FOR THIS PATENT. L10 ANSWER 16 OF 18 USPATFULL on STN 78:61415 USPATFULL ΑN TΙ Stabilizer system for stabilizing styrene polymers ΙN Gilg, Bernard, Saint-Louis, France Muller, Helmut, Binningen, Switzerland

```
Rody, Jean, Basel, Switzerland
       Ciba-Geigy Corporation, Ardsley, NY, United States (U.S. corporation)
PΑ
PΙ
       US 4123418
                                19781031
ÎΑΙ
                                19751205 (5)
       US 1975-638125
       Continuation-in-part of Ser. No. US 1974-461188, filed on 9 Apr 1974,
RLI
       now abandoned
       CH 1973-5753
                           19730419
PRAI
DT
       Utility
FS
       Granted
LN.CNT 913
       INCLM: 260/045.800NT
INCL
       INCLS: 260/045.800N
       NCLM: 524/091.000
NCLS: 524/102.000
NCL
IC
       [2]
       ICM: C08K005-34
       260/45.85; 260/45.8NT; 260/45.95; 260/45.8N; 252/404; 252/407
EXF
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L10 ANSWER 17 OF 18 USPATFULL on STN
       78:47259 USPATFULL
ΑN
ΤI
       Stabilizer system and its use for stabilizing styrene polymers
       Gilg, Bernard, Saint-Louis, France
Muller, Helmut, Binningen, Switzerland
ΙN
       Rody, Jean, Basel, Switzerland
       Ciba-Geigy Corporation, Ardsley, NY, United States (U.S. corporation)
PΑ
PΙ
       US 4110304
                                19780829
AΙ
       US 1975-638226
                                19751205 (5)
RLI
       Continuation-in-part of Ser. No. US 1974-461188, filed on 12 Apr 1974,
       now abandoned
       CH 1973-5753
                           19730419
PRAI
       Utility
DТ
       Granted
LN.CNT 1030
       INCLM: 260/045.800A
       INCLS: 252/404.000; 252/407.000; 260/045.800N; 260/045.850B;
               260/045.850V; 260/045.800NT; 260/045.950F; 260/045.900NC
               524/091.000
NCL
       NCLM:
       NCLS: 252/404.000; 252/407.000; 524/094.000; 524/099.000; 524/100.000
IC
       [2]
       ICM: C08K005-34
       260/45.85B; 260/45.85V; 260/45.85A; 260/45.8N; 260/45.8NT; 260/45.95F;
       260/45.9NC; 252/404; 252/407
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L10 ANSWER 18 OF 18 USPATFULL on STN
       77:35769 USPATFULL
AN
T \cdot I
       Stabilized epoxy resins
ΙN
       Randell, Donald Richard, Stockport, England
       Cook, Barry, Manchester, England
       Chalmers, Alexander Michael, Cheadle, England
PΑ
       Ciba-Geigy Corporation, Ardsley, NY, United States (U.S. corporation)
       US 4033928
PΙ
                               19770705
       US 1975-564185
ΑI
                                19750401 (5)
       GB 1974-16127
PRAI
                           19740411
DT
       Utility
FS
       Granted
LN.CNT 1237
       INCLM: 260/045.800N
       INCLS: 260/045.800NE; 260/045.800NZ
NCL
       NCLM:
               523/445.000
       NCLS: 523/451.000; 523/461.000
```

IC [2]

ICM: C08K005-00

EXF 260/45.8NE; 260/45.8NZ; 260/45.75K \*CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s exendin 4?

L18 141 FILE MEDLINE

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

156 FILE EMBASE

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

## TOTAL FOR ALL FILES

L20 297 EXENDIN 4?

You have entered a truncated stem which occurs in too many terms. Make the stem longer and try again. For example, if your original term was 'degr?' to search for variations and the abbreviation for 'degradation', you could replace it with the expression '(degrdn OR degrad?)'. If your search term was numeric, e.g., 'C>5', reduce the size of the range.

=> s 120 and (dicarboxyl? or methylene)

0 FILE MEDLINE

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

O FILE EMBASE

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

TERM '4?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

## TOTAL FOR ALL FILES

0 L20 AND (DICARBOXYL? OR METHYLENE)

You have entered a truncated stem which occurs in too many terms. Make the stem longer and try again. For example, if your original term was 'degr?' to search for variations and the abbreviation for 'degradation', you could replace it with the expression '(degrdn OR degrad?)'. If your search term was numeric, e.g., 'C>5', reduce the size of the range.

=> log v

COST IN U.S. DOLLARS

SINCE FILE TOTAL SESSION ENTRY

FULL ESTIMATED COST

82.47 120.22

STN INTERNATIONAL LOGOFF AT 16:13:50 ON 16 JUN 2004